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Oral Liquids Pharmaceutical Dosage Forms

K.MALLESWARI
M.Vennela, NalandaInstitute of Pharmaceutical Sciences, Kanttepudi, Sattenapalli, Guntur.
Dr. Ramabramha Reddy

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ABSTRACT
Pharmaceutical liquid dosage forms are the liquid solutions that can be ingested, applied topically, or administered intravenously. These dosage forms are made up of a mixture of active medicines and excipients that produce a quick beginning of action after ingestion and provide the best therapeutic response in a given population. Pharmaceutical liquid dose forms are helpful and efficient for pediatric, elderly, and comatose patients who have difficulty swallowing solid dosage forms such as pills, capsules, and other medications. As a result, pharmaceutical liquid dosage forms are extremely important in the treatment and management of a wide range of disorders around the global. This article covers a wide range of topics related to pharmaceutical liquid dosage forms, including classification, benefits and drawbacks, excipients utilised in pharmaceutical liquid dosage forms, solubility enhancement techniques, and some of the instruments used to improve mixing.

Keywords: Solubility; Bioavailability; Excipients; Lipophilic

I. INTRODUCTION

Pharmaceutical liquid dosage forms are those preparations that contains a combination of active drugs and excipients (emulsifying, dispersing, solubilizing, stabilizing, suspending, wetting, thickening agent, preservative, sweetening agent, flavoring agent, and colorings agent) that are dissolved or suspended in appropriate solvents and used as a drug or medication . It is the simplest type of pharmaceutical preparations for high absorption of medicinal drugs and rapid onset in which two components are enhanced to complete a liquid dosage form solute (a component that dissolves) and solvents (the medium in which the solute will dissolve). In pharmaceutical liquid preparations, parenteral routes are available in sterile forms, whereas oral liquids are non-sterile and can be administered via oral or parenteral routes (Injectable, inhalation, otic, tropical, nasal and ophthalmic). With the help of a chart, the classification of liquid dosage forms is presented below. Monophasic liquid dosage forms are the liquid solutions that comprise two or more components in a single phase. True solutions, which are homogeneous mixtures created by dissolving solute in long-term solvents, are also known as true solutions [1]

SOLUTIONS

Solid materials are dissolved in an appropriate solvent, which are homogeneous mixture containing one or more chemical compounds. Solutions are one of the oldest dosage forms and are made by dissolving a solid, liquid, or gas into a solvent in which the solute molecules are dissolved into a solvent such as water, alcohol or carbonated beverages.

SYRUP

Syrup is a sugar-in-water saturated aqueous solution with or without medicinal, ingredients. Syrups have a high percentage of sucrose (66.7% w/w I.P. and 85% w/v USP). Prepare sucrose 66.7% w/w syrup in filtered water, stirring constantly while heating. It's crucial not to let the temperature climb above 1600°C while heating. After cooling, it's kept in a cool, dry area in a tightly sealed container to keep moisture and foreign particles out. Vitamins, sedatives, saline medicines, and antibiotics all use syrups in their compositions [2].

LINCTUS

Linctus is a viscous, monophasic liquid solution with a high syrup concentration that is used to treat cough and sore throat. It's made by dissolving citric acid in chloroform, adding peppermint water, amaranth solution, and syrup (as a carrier) to reach the desired volume. However, the majority of linctus comprises chemicals that have expectorant, sedative, and antibacterial properties.

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ELIXIRS

An elixir is a sweet fragrant liquid mixture that is administered orally for medical purposes. It contains a variety of active substances, including ethyl alcohol, propylene glycol, water, glycerin, and flavoring agents, all of which are necessary for elixir manufacture. Medicated elixirs and non-medicated elixirs are the two types of elixirs available. Non-medicated elixirs are used as vehicles or solvents for medicated elixirs, which include potent medications as antihistaminic, antibiotics, hypnotics, and sedatives, and should be kept in a light-resistant, firmly closed container away from sunlight.

GARGLE

Gargles are aqueous concentrated solutions that are used to treat throat infections by coming into touch with the mucus membrane in the buccal cavity. Gargles are delivered in a concentrated form, but when used, they are diluted with warm water. Gargles are kept in an airtight jar with a plastic screw cover [3].

MOUTHWASH

Mouthwashes are aqueous solutions with a pleasant taste and odour that are used to keep the buccal cavity clean and deodorized. Alcohol, glycerin, antimicrobial, colouring, and flavoring agents are all found in mouthwashes. Food particles caught deep inside the throat and mucous in the mouth can be eliminated with the help of mouthwashes with strong flavors and alcohol, which function by producing cough. Mouthwashes come in a variety of flavors, including antibacterial and anti-plaque mouthwashes, anti-cavity mouth rinses, and more. The antiseptic mouthwashes eliminate the bacterial plaque that causes bad breath, caries, and gingivitis, while the fluoride-containing mouthwashes protect against tooth decay. It's primarily used for dental hygiene. In general, some firms suggest that when mouthwash is used, you should not drink water right away. However, mouthwashes are ineffective in removing plaque and bad breath, thus brushing and flossing are required

LOTIONS

Lotions are liquid preparations for application to the skin's surface. Lotions are applied to the skin's surface with cotton wool for purposes of protection, such as cooling and relaxing. Antiseptic, antibacterial, antifungal, moisturising, and protective substances are prescribed by dermatologists to treat or prevent skin problems .

LINIMENT

Liniment is a liquid dose form of medication that is applied to the affected area with friction or rubbing action. Liniments are a blend of substances with qualities such as analgesic, relaxing or stimulating. These should only be used on the outside of the body and should not be used on broken skin.

NASAL DROPS

Nasal drops are liquid or greasy solutions that are sprayed into the nostrils with a dropper. Antiseptics, local analgesics, and vasoconstrictors are all present in these solutions. The droplets are usually watery rather than greasy. Nasal drops are isotonic because they have a neutral pH and a viscosity that is similar to nasal secretions, thanks to the usage of methyl alcohol.

EAR DROP

Ear drops are solutions made from water, glycerin, or propylene glycol that are infused into the ear using a dropper. They are used to clean the ear canal, soften wax, and treat minor infections. When viewed under a microscope under suitable conditions of visibility, ear drops are clear solutions that do not include any particles . Ear drops are also available as suspensions, which generate sediment that disperses widely when the container is shaken and stays disseminated for a long time.

THROAT PAINTS

Throat paints are the viscous liquid dosage form of medicaments which are used for the purpose of mouth and throat infections. Glycerin is typically used as a base in significant amounts to ensure that the medicine stays in contact with the mucous membrane for a long time and has a pleasant flavour[4].

EYE DROPS

Eye drops are ocular dosage forms of medications with drawbacks such as limited availability, frequent administration, pharmaceutical outflow through tears, unpredictability of dosages, and lacrimal fluid. The inherent physiology of the eye continues to make ocular drug distribution difficult. The efficient removal mechanism at the site of action (rapid tear turnover, blinking) and low corneal permeability combine to diminish the efficacy of ophthalmic formulations and restrict drug bioavailability to less than 5%.

BIPHASIC LIQUID DOSAGE FORMS

Biphasic liquid dosage forms are ones that have two phases in them. This comprises the medicine that

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has been dissolved as well as the solvent (vehicle). There are two types of biphasic liquid dosage forms.
• Suspension
• Emulsion

SUSPENSION

Suspensions are biphasic liquid dosage forms of medication in which the internal phase is uniformly distributed with finely divided solid particles in a liquid dispersion medium over a period of 0.5 to 5 minutes. In pharmaceutical solutions, solid particles act as a disperse phase, while liquid vehicles act as a continuous phase. The external phase, also known as the suspending medium, . Pharmaceutical suspension formulations are done for the following reasons.
• To improve the drug stability of the suspensions.
• To reduce the bitterness.
• The medication is insoluble in the delivery medium in this formulation.
• To achieve long term medication release (sustained release).

CLASSIFICATION OF SUSPENSION:

Suspensions are categorised using the following framework:
• Determined by administration route
• Oral
• Parenteral
• Topical
• Based on the nature of solid particles electro kinetics
• Flocculated suspension
• Deflocculated suspension

ORAL SUSPENSIONS

For oral administration, an oral suspension consists of undissolved particles and active substances suspended in sweetening, flavoring, or viscous vehicles with therapeutic agents. Oral suspensions are commonly used to treat oral fungal infections. "Oral suspensions allow for dose flexibility and are cost-effective when a patient requires dose titration, however many pharmaceutical medications are not available as oral suspensions. Insoluble components are suspended in a dispersion media with suspending agents to create oral suspensions. Suspending agents are used to help disperse powders evenly throughout the preparation and avoid particle flocculation [5].

ADVANTAGES OF ORAL SUSPENSIONS

• It must be pleasant as well as stable.
• There should be no gritty particles in it.
• Particles that are dispersed should not settle easily.

PARENTERAL SUSPENSIONS

Parenteral suspensions are sterile preparations that are intended to be administered directly into the systemic circulation of people . Parenteral suspensions are insoluble medication particles dispersed in a heterogeneous system that must be resuspended in an aqueous or vegetable oil vehicle before being administered to patients.

IDEAL CHARACTERISTICS OF PARENTERAL SUSPENSION

• Parenteral suspensions should be small and uniform.
• Particle re-suspension becomes very simple.
• The viscosity of the suspension determines its injectability.
• Sterility of the product during usage and storage.
• After shaking, dispersed particles do not settle quickly.
• During the shelf life of the cake, it does not form.
• The elegance of the product should be preserved throughout its shelf life.
• These are non-irritating and isotonic. Parenteral suspensions have a number of advantages
• The parenteral suspensions are utilised therapeutically and are insoluble in ordinary solvents.
• The dose forms make the suspensions more resistant to hydrolysis and suspensions.
• Controlled release formulation is possible in parenteral suspensions.
• There's a chance of a hepatic first-pass effect. Disadvantages of parenteral suspensions

DISADVANTAGES OF PARENTERAL SUSPENSIONS

• Manufacturing difficulty: Crystallization, particle size reduction, wetting, and sterilising operations are facilitated, which are necessary to maintain aseptic manufacturing conditions.
• Formulation difficulty: Suspending agents, viscosity inducing agents, wetting agents, stabilisers, and preservatives for this form of parenteral suspension are challenging to choose.
• In this dosage type, physical stability is extremely difficult to maintain.
• At the time of administration, the dose is not uniform.

Factors affecting medication release from parenteral suspensions
• Injectable suspension formulations are approved by parenteral suspensions; the medicine is soluble in biological fluids at the injection site.

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• Because of injectability and syringeability, these suspensions are frequently diluted due to their viscosity limitations.
• Pka of the medicine and the rate at which solids from its dose forms dissolve [6].

TROPICAL SUSPENSIONS

Tropical suspensions are liquid treatments that contain solid particles suspended in a liquid carrier for skin application.

TROPICAL DRUG DELIVERY

A tropical drug delivery system is a localised delivery system that allows therapeutic chemicals to be delivered locally via the skin to treat cutaneous problems. Skin infections are commonly treated using tropical suspensions. Tropical suspensions are designed to provide effective and efficient medication action as well as an influence on the site of action.

EMULSION

A biphasic liquid dosage form of a drug is an emulsion, which is made up of two immiscible liquids, one of which is the dispersed phase and the other the continuous phase. Emulsions are a thermodynamically unstable system that must be stabilised by adding a third component called an emulsifier. Emulsifiers stabilise the system by forming a thin film around the dispersed phase globules, which range in size from 0.1 to 100 micrometers in diameter [7].

TYPES OF EMULSION

The two basic types of emulsions such as
• O/W (oil dispersed in water)
• W/O (water dispersed in oil).

OIL-IN-WATER EMULSIONS (O/W)

Pharmaceutical emulsions are made up of a mixture of oil droplets scattered throughout the aqueous phase. Fats and oils for oral administration are always manufactured as oil-in-water (O/W) emulsions shows in figure 2, whether as carriers for oil-soluble medications or as medicines in their own right. They're non-greasy and easy to wipe away from the skin's surface [30]. They are applied physically to provide a cooling effect and internally to the mask the oil's unpleasant taste.

WATER-IN-OIL-EMULSIONS (W/O)

W/O emulsions (water-in-oil emulsions) are medicinal emulsions in which water is scattered as globules in oil continuous phase shows in figure 3. Water-in-oil emulsions have an occlusive action, which hydrates the stratum corneum and prevents the evaporation of eccrine secretions. They're oily but not watersoluble, and they're used to maintain moisture from evaporating from the skin's surface while cleansing it of oil-soluble dirt.
Example: Cold cream.

SELECTION, QUALITIES AND FUNCTIONS OF EXCIPIENTS

Excipients are substances in a formulation that are not active compounds. They can be natural or synthetic substances added with the drug for long-term stability, formulations including the drug, or therapeutic augmentation of the drug in the final dosage form. Excipients are non-active or inactive chemicals that are added to pharmaceutical compositions during the manufacture of dosage forms. They have no therapeutic effect but are required to alter the drug's and dosage form's function. Because they are inert in nature, they have no pharmacological impact.

It mostly aids in the manufacturing process by preventing nonstick qualities and maintaining in vitro stability, such as aiding flow-ability or aggregating over time. As a result, excipients are an essential component of pharmaceutical dosage forms, and they are included in higher proportion in most formulations than the medication. Although excipients are considered inert substances, several of them have been discovered to have a direct impact on dissolution rate and medication absorption. Some excipients were discovered to have some efficacy in terms of promoting penetration into tumor cells. Specific investigations validated concerns about the prevalence of some negative effects connected with the presence of certain types of excipients, such as sugar and lactose; paraben and menthol are linked to hyperglycemia, stomach cramps, hypersensitivity reactions, and laryngeal spasms in newborns, respectively.

SELECTION OF EXCIPIENT

It depends on upon its physicochemical properties, characteristics of active drug and route of drug administration. Regulatory acceptance, material consistency, source, cost and availability, stability and compatibility issues, pharmacokinetic parameters, permeation characteristics, segmental absorption, behavior, drug delivery platform, intellectual property issues, and so on are all factors to consider. Knowledge of API, excipients, their interactions, and process parameters is essential for a successful pharmaceutical formulation.

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IDEAL QUALITIES OF EXCIPIENTS

• Excipients perform well in their intended applications.
• They have to be physiologically inactive.
• They must be physically and chemically stable.
• They should be less affected by machinery and processes.
• They have to be non-toxic.
• They must be acceptable in terms of organoleptic qualities.
• There is no effect on medication bioavailability.
• Excipients must not include pathogenic bacteria.
• They must meet the requirements of the regulating agency.
• They must be cost-effective.

EXCIPIENTS UTILISED IN LIQUID DOSAGE FORM FORMULATION

Excipients are categorised according to the function they perform; however, different excipients respond differently at different concentrations, and one excipient might be employed for numerous purposes depending on the dosage form's requirements. Oral liquid formulations are made by mixing various chemicals to accomplish activities such as wetting and solubilization, stability, and the addition of appropriate colour, taste, and viscosity. Compatible, non-reactive, and stable formulations are required.

The following excipients are commonly used in liquid formulations:

• Vehicles
• Solubilizers
• Preservatives
• Stabilizers
• Organoleptic agents

VEHICLES

SOLVENTS

In liquid pharmaceutical formulations, vehicles are important components that serve as a base for dissolving or dispersing drugs and other excipients. They work by breaking bonds and reducing effective charge on ions, increasing solute-solvent attraction forces, which eventually outnumber solute-solute and solvent-solvent attraction forces. Water, hydro-alcoholic liquid systems, polyhydric alcohols, acetic acid, ethyl acetate, and buffers are examples of such substances. Thin liquids, thick syrupy liquids, mucilage, and hydrocolloid bases are all possibilities . Vegetable oils, mineral oils, organic oily bases or emulsified bases are examples of oily vehicles. Co-solvents

CO-SOLVENTS

Co-solvents are organic solvents that are water miscible and utilised in liquid medicine formulations to boost the solubility of weakly water soluble compounds or to improve the chemical stability of a drug. A co-solvent boosts a drug's solubility. The dielectric constant of an ideal co-solvent should be between 25 and 80. A water/ethanol blend is the most generally utilised solution that will handle this range. When administered for oral or parental use, it should not cause toxicity or irritancy. Sorbitol, glycerol, propylene glycol, and syrup are some of the other co-solvents.

SOLUBILIZERS

Solubilizers are a type of fungicide that to improve the drug's solubility, make the following pH adjustments: By incorporating a buffer into the formula. To control potential pH variations, buffers act by binding hydrogen formulations. In acids, buffers bind hydrogen ions, while in bases, they donate hydrogen ions. The acid-base form's suitability for use in oral liquids, the stability of the medicine and excipients in the buffer, and the buffer's compatibility with the container should all be considered when choosing a suitable buffer. The possible reactivity between excipients and medication is determined by the stabilising impact of buffers.

Carbonate, citrate, tartarate, and phosphate salts, for example, may precipitate with calcium ions to generate sparingly soluble salts. Temperature, ionic, strength, dilution, and the number and kind of co-valents present are all factors that can change the pH of a solution. The pH of acetate buffers, for example, is known to rise with temperature, but the pH of boric acid buffers is known to fall with temperature. It's crucial to understand that the medicine in solution might act as a buffer. If the drug is a weak electrolyte like salicylic acid or ephedrine, adding a base or acid will produce a situation where the drug can operate as a buffer.

EXAMPLE : phosphate buffers, acetate buffers, citric acid phosphate buffers etc.
Co-solvency is achieved by mixing a water miscible solvent with a medication that has a high solubility. Co-solvent is a type of solvent. When a Complexing agent is added to a solution, it forms a complexation with the drug.

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WETTING AGENT

Wetting agents and surfactants are commonly utilised in pharnmaceutical formulations; they are air adsorbed at solid particle surfaces and keep them away from vehicles, allowing the vehicle to penetrate the pores and capillaries of the particles. Mineral oils are widely used as wetting agents in non-aqueous based formulations because hydrophobic medication particles are difficult to wet even after adsorbed air has been removed. In such instances, it is vital to minimise the surface. The particles and the liquid vehicles are in a state of tension. Branched hydrophobic chains with core hydrophilic groups or short hydrophobic chains with hydrophilic end groups make up surface active compounds that operate as wetting agents. One of the most often utilised surface-active chemicals as a wetting agent is sodium lauryl sulphate [33]. When dissolved in water, it lowers the water's contact angle and aids in the spread of water across the particles' surfaces, removing the air layer at the surface and replacing it with the liquid phase.

PRESERVATIVES

A major issue with aqueous-based liquid dosage forms is microbial contamination. In such instances, the use of preservatives becomes unavoidable to inhibit the growth of microorganisms during production and storage. In fact, developing a preservative-free formulation is desirable to avoid the negative effects of these excipients. Most of the preservatives are bacteriostatic rather than bactericidal and come in both acid and non-acid forms . The following conditions must be met by preservatives: Efficacious against a wide range of bacteria.

For the duration of the product's life, it must be physically, chemically, and microbiologically stable.

TYPES OF PRESERVATIVES

• Acidic: Phenol, benzoic acid, sorbic acid
• Neutral preservatives: Chlorobutanol, benzyl alcohol
• Quarternary ammonium compounds : Benzalkonium chloride.

STABILIZERS

In liquid dosage forms, oxidation, photolysis and dehydration are frequent changes. Because of their low activation energies, oxidation and photodecomposition of drugs are relatively prevalent mechanisms of drug disintegration and are difficult to manage. The oxidation reaction is triggered by trace levels of contaminants that are typically present in the medicine or excipient. When drugs are continuously exposed to an open environment in their reduced form, they demonstrate greater vulnerability. Because ionised versions of these me at specifc PH.

PHYSICAL STABILITY

Throughout its shelf life, a stable formulation maintains its viscosity, colour, clarity, taste, and odour. Colour can be determined via Spectrophotometry. Measurement of turbidity or light scattering equipment can be used to estimate clarity. Viscometers are used to measure viscosity. A pharmaceutical investigator or a panel of unbiased, taste-sensitive individuals can determine taste and odour. pH, temperature, ionic strength, solvent effects, light, and oxygen all have an impact on the formulation's chemical stability.

Buffering agents, antioxidants, and proper packaging can all help to prevent instabilities (eg: use of amber bottle for light sensitive products).

Antioxidants operate as chain terminators, reacting with free radicals in solution to halt the proliferation of free radicals. To achieve a synergistic impact, chelating agents and antioxidants are frequently combined. Because several of these chemicals operate at different stages of the oxidative process, this is the case. Products having a disagreeable odour, taste appearance, ppt, discoloration, or even a minor loss of activity result from oxidation of formulation components. Unsaturated oils/fats, chemicals containing aldehyde or phenolic groups, colours, flavours, sweeteners, plastics, and rubbers, the latter of which is utilised in product containers, are all susceptible to oxidation.

Acetone sodium bisulfite, acetylcysteine, ascorbic acid, and thiourea are among examples.

Emulsifying chemicals that prevent dispersed globules from coalescing. It reduces interfacial tension by forming barriers at the interface. Example: sodium lauryl sulphate, cetrimide, and macrogol.

ANTIFOAMING AGENTS

Foam development during manufacturing procedures or when re-forming liquid dosage forms can be undesirable and disruptive. Antifoaming chemicals work by reducing the surface tension and cohesive binding of the liquid phase, which prevents the production of stable foams. Simethicone, organic phosphates, alcohols, paraffin oils, and other similar substances are examples.

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SUSPENDING AGENTS

Agents for Suspension and Viscosity Enhancement: One of the most important aspects of preparing a pharmacological suspension is choosing the right suspending agent. Suspending agents cause particle settling by imparting viscosity. The intended rheological property supendability in the system, chemical compatibility with other excipients, pH stability, hydration time, repeatability, and cost are all considerations to consider when choosing the right suspending and viscosity boosting agent. Example: Clays, natural gums, and synthetic gums.

For improved benefits, these excipients are frequently used in combination in numerous formulations. Humectants are hygroscopic chemicals that help to prevent aqueous vehicles from evaporating from dosage forms. These excipients are utilised in aqueous suspensions and emulsions for external application at a concentration of 5%. They're also used to keep the product from drying out after it's been applied to the skin, as well as to keep the product from drying out after it's been opened. It also aids in preventing cap-locking caused by condensation on the container-neck closures during the initial opening. Example: Propylene glycol, glyerol, and polyethylene glycol.

Prevent caking with flocculating chemicals. The zeta potential of dispersed particles is reduced when an electrolyte is added. Example, starch with sodium alginate.

Chelating agents are chemicals that form complexes with metal ions in order to activate their catalytic activity in the oxidation of pharmaceuticals. These agents can build complexes with the drug that involve more than one bond; a complex compound is one that has one or more rings in its structure. Protect the medication from catalysts that speed up the oxidation process. Example: Disodium EDTA, dihydroxy ethyl glycine, citric acid, and tartaric acid . Properties of the organoleptic system.

Flavoring agents are introduced to the solvent or vehicle component of the formulation where they are most soluble or miscible in liquid medicinal formulations.

Water soluble flavours are added to the aqueous component of a formulation, while flavours that are weakly water soluble are applied to the alcoholic or non-aqueous solvent component. Care must be taken to keep flavorants in solution in a hydro-alcoholic or other multi-solvent system. This is performed by keeping the flvorants solvent at a safe level.

SWEETENING AGENTS

Sucrose increases the viscosity of liquids while also providing a nice mouth feel. Sweetening chemicals such as sorbitol, mannitol, saccharin, and aspartame, as well as sugars such as sucrose and fructose, are included in the term sugar free solution. A number of artificial sweetening compounds, in addition to sucrose, have been utilized in food and medications over the years. The FDA has questioned the safety of several of these ingredients, such as aspartane, saccharin, and cyclamate, and has placed restrictions on their use and sale. In reality, the FDA outlawed the use of cyclamates in the United States in 1969. Sucralose is widely used because of its exceptional sweetness, non-cryogenic properties, low calorie content, and gaining regulatory acceptance, however it is quite costly.

DE-COLORATION AGENT

It's important to distinguish between agents that are naturally colored and those that are used as colorants. According to the D&C Act 1940, colours used in liquid dosage forms must be FDA certified. Sulphur (yellow), riboflavin (yellow), cupric sulphate (blue), ferrous sulphate (bluish green), cyanocobalamin (red), and red mercuric iodide (vivid red) are examples of substances that have inherent colour and are not considered medicinal colorants in the traditional sense. Although the majority of pharmaceutical colorants are synthetic today, a few are derived from natural mineral and plant sources. Red ferric oxide, for example, is blended in small amounts with zinc oxide powder to give calamine its distinctive pink colour, which is meant to complement the skin tone when applied. Because particular age groups seem to favour certain flvours, the age of the intended patient should also be considered when choosing a flavoring agent. Children like sweet candy-like preparations with fruity flavours, whereas adults prefer a less sweet preparation with a sour flavour rather than a fruit flavour.

SOLUBILITY ENHANCEMENT TECHNIQUES

Surfactants The traditional strategy to solubilizing a poorly soluble chemical is to lower the interfacial tension between the surface of solute e and the surface of the solvent to improve wetting and salvation contact. Surfactants such as Polyglycolyzed glycerides, Tweens, Spans, Polyoxyethylene stearates, and synthetic block

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copolymers such as Poly (propylene oxide)-poly (ethylene oxide)-poly (propylene oxide)-poly (ethylene oxide)-poly (ethylene oxide)-poly (ethylene oxide)-poly (ethylene oxide)-poly (ethylene. The use of amphiphilic surfactants improves drug solubility by lowering surface tension between the drug and the solvent, improving wetting qualities, and micellar solubilization[7].

pH ADJUSTMENTS

Increasing the water solubility of ionizable substances is as simple as adjusting the pH of the microenvironment to change the ionisationbehaviour. Ionization of a chemical is reliant on the pH of the media and the pKa of the medication, according to the pHpartition theory and the Handerson- Hasselbach equation. In situ salt production can also be caused by a change in the ionic environment. For unionised chemicals, however, this salt production is impossible . In the gastrointestinal tract, the produced salts may react with the relevant acid or base forms.

SALT FORMATION

For decades, salt production of poorly soluble medication candidates (weak acids and bases) has been used to improve solubility. It works effectively in both parenteral and other liquid formulations as well as solid dose forms. Between 1995 and 2006, the FDA approved over 300 novel chemical entities for marketing, 120 of which were salt forms. Furthermore, hydrochloric acid was used to produce 54 of the 101 approved salts of basic medicines, indicating that hydrochloride was the most common salt type .An acidic or basic drug's water solubility as a function of pH determines whether the chemical will form appropriate salts [8]. The pH-solubility interrelationships also determine what counter ions are required to create salts, how quickly the salts dissociate into their free acid or basic forms, how salts dissolve under varied GI pH conditions, and if common ion influences salt solubility and dissolution rate.

CO-SOLVENTS

A co-solvent system is a concoction of miscible solvents that is commonly employed to dissolve lipophilic medicines. Polyethylene glycol 400 (PEG 400), ethanol, propylene glycol, and glycerin are currently the water-soluble organic solvents. For example, Pfizer's Procardia (nifidipine) soft gelatin capsules contain glycerin, peppermint oil, PEG 400, and sodium saccharin. Long-chain triglycerides (peanut oil, corn oil, soybean oil, sesame oil, olive oil, peppermint oil, hydrogenated vegetable oil, and hydrogenated soybean oil), medium-chain triglycerides (Miglyol 812), beeswax, d— tocopherol (vitamin E), and oleic acid are among the water insoluble solvents.

Progesterone, a water-insoluble steroid that is soluble in peanut oil, is a commercially accessible example of this method .

POLYMERIC MODIFICATION

Polymorphs are distinct crystalline forms of a medication that may have diverse characteristics. Physical and chemical stability, shelf-life, melting point, vapour pressure, intrinsic solubility, dissolving rate, shape, density, and biological activity, as well as bioavailability, may differ amongst polymorphs . Metastable crystalline polymorphs are related with higher energy, increased surface area, and thus solubility and bioavailability and efficacy, when compared to stable, unstable, and metastable crystalline polymorphs . It is better to convert drugs from crystal forms to metastable or amorphous forms in order to increase bioavailability. During manufacturing and storage, however, the possibility of a conversion of the high energy amorphous or metastable polymorph into a low energy crystal form with limited solubility cannot be ruled out. To ensure reproducible bioavailability of the product across its shelf-life under a variety of real-world storage settings, it is desirable to design the most thermodynamically stable polymorph of the medicine[9].

PARTICLE SIZE REDUCTION

Micronization or nanonization is one of the most promising techniques for improving lipophilic drug bioavailability by increasing surface area and saturating solubility by reducing particle size to sub-micron levels [43]. Particle size is a vital metric that should be closely monitored during any formulation's preformulation investigations. Although particle size reduction is a successful approach to increase solubility, if it is not controlled and optimized, it might cause recrystallization and re-aggregation of the drug during storage. As a result, a thorough investigation of particle size and physical stability is required.

CO-PRECIPITATION

Weak basic medicines, such as prochlorperazine maleate, have strong solubility in acidic pH but not in alkaline pH, and when a standard formulation containing weak base is

administered orally, precipitation of poorly soluble free base occurs within the formulation in the intestinal fluid. The medicine is no longer able to release from the formulation, resulting in a decrease in bioavailability. This problem can be solved by using a co-evaporate system that combines a carrier with a solubilizing effect in alkaline intestinal fluid that can operate in the microenvironment, immediately surrounding the drug particle, and polymers to control the dissolution rate in order to formulate dosage forms with maximum bioavailability and controlled release of weak bases [10].

SOLVENT DEPOSITION/EVAPORATION

In this procedure, the medication is dissolved in a transparent solution such as methylene chloride. Stirring disperses the carrier in the solution, while evaporation under temperature and pressure removes the solvent. After that, the resulting mass is dried, crushed, and sieved. The increased dissolving rate is attributed to the smaller particle size of the medication deposited on the carrier and the carrier's increased wettability of the particles. Ordered mixing is defined as a method of preparing ordered units in a mix in such a way that the ordered unit is the smallest feasible sample of the mix and has a composition that is nearly identical to all other ordered units in the mix. Ordered mixing produces a near-perfect mix and can be achieved in a variety of ways, including mechanical means, adhesion, coating, and other techniques. The carrier particle must dissolve quickly in order to deliver a tiny particulate suspension of drug particles, which is a need for fast dissolution from an ordered mixture. Dissolution rates are lowered with higher drug concentrations, especially at loadings over monolayer coverage .

STREAM-ASSISTED GRANULATION

Steam can be used instead of water in wet granulation since it allows for a faster diffusion rate into the powder and a better thermal balance throughout the drying process. Water produces a heated thin layer after condensation of steam, requiring only a small amount of extra energy to evaporate and evaporating more easily . In a wet granulation process, using steam instead of liquid water can significantly reduce the amount of water utilised and, as a result, the total operational time.

DIRECT COMPACTION

Polymers such as HPMC and drugs are dry-blended, compressed into slugs, and then processed into a granular powder in this procedure. To overcome the difficulties of solid dispersion by these methods, the approach results in increased dissolving rate of low water soluble pharmaceuticals without the use of solvent or heat addition. This method is also less expensive and faster. In contrast to a physical mixture, where the drug and polymer particles may rapidly disperse and be separated in the dissolution medium, compaction processes are thought to be particularly effective at enhancing the rate of drug dissolution because the drug particles are kept in direct contact with the polymer particles during drug dissolution [11].

LIQUISOLID COMPACTS

Liquid Compacts are powdered formulations of liquid pharmaceuticals that can be compressed. Oily liquid medications and solutions or suspensions of water insoluble drugs carried in suitable nonvolatile solvent systems are referred to as "liquisolid medication." By blending a liquid medication with specified powder excipients such as the carrier and coating material, a liquid medication can be turned into a dry, non-adherent, free-flowing, and compressible powder . Surfactants like tweens are used to help poorly soluble medications dissolve in water [12].

II. CONCLUSION

In today's era, the world population is suffering from several diseases as the result the number of increasing patients having difficulties in swallowing tablets and capsules. In that case liquid dosage forms works effectively in both older and pediatric patients. There is creates a problem for the healthcare professionals, especially for the pharmacists who is often required to provide a monophasic and biphasic liquid preparations. According to an extensive survey based on large scale on literature and investigation of 83 liquid dosage form comforted that stability consideration were conformed only 7.2 of liquid dosage forms, extemporaneously prepared from the commercially available products such as liquid dosage forms which are sketched to provide the maximum therapeut.

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